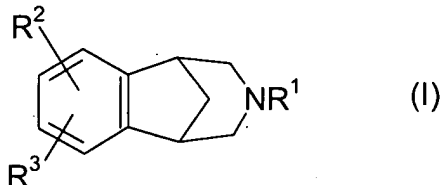


IN THE CLAIMS (37 CFR 1.121 Revised)

1. (currently amended) A pharmaceutical composition comprising a compound of the formula



R¹ is hydrogen, (C₁-C₆)alkyl, unconjugated (C₃-C₆)alkenyl, XC(=O)R¹³, benzyl or -CH₂CH₂-O-(C₁-C₄)alkyl;

R² and R³ are selected, independently, from hydrogen, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, hydroxy, nitro, amino, halo, cyano, -SO_q(C₁-C₆)alkyl wherein q is zero, one or two, (C₁-C₆)alkylamino-, [(C₁-C₆)alkyl]₂amino-, -CO₂R⁴, -CONR⁵R⁶, -SO₂NR⁷R⁸, -C(=O)R¹³, -XC(=O)R¹³, aryl-(C₀-C₃)alkyl- or aryl-(C₀-C₃)alkyl-O-, wherein said aryl is selected from phenyl and naphthyl, heteroaryl-(C₀-C₃)alkyl- or heteroaryl-(C₀-C₃)alkyl-O-, wherein said heteroaryl is selected from five to seven membered aromatic rings containing from one to four heteroatoms selected from oxygen, nitrogen and sulfur, and X²(C₀-C₆)alkoxy-(C₀-C₆)alkyl-, wherein X² is absent or X² is (C₁-C₆)alkylamino- or [(C₁-C₆)alkyl]₂amino-, and wherein the (C₀-C₆)alkoxy-(C₀-C₆)alkyl- moiety of said X²(C₀-C₆)alkoxy-(C₀-C₆)alkyl- contains at least one carbon atom, and wherein from one to three of the carbon atoms of said (C₀-C₆)alkoxy-(C₀-C₆)alkyl- moiety may optionally be replaced by an oxygen, nitrogen or sulfur atom, with the proviso that any two such heteroatoms must be separated by at least two carbon atoms, and wherein any of the alkyl moieties of said (C₀-C₆)alkoxy-(C₀-C₆)alkyl- may be optionally substituted with from two to seven fluorine atoms, and wherein one of the carbon atoms of each of the alkyl moieties of said aryl-(C₀-C₃)alkyl- and said heteroaryl-(C₀-C₃)alkyl- may optionally be replaced by an oxygen, nitrogen or sulfur atom, and wherein each of the foregoing aryl and heteroaryl groups may optionally be substituted with one or more substituents independently selected from (C₁-C₆)alkyl optionally substituted with from one to seven fluorine atoms, (C₁-C₆)alkoxy optionally substituted with from two to seven fluorine atoms, halo, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, hydroxy, nitro, cyano, amino, (C₁-C₆)alkylamino-, [(C₁-C₆)alkyl]₂amino-, -CO₂R⁴, -CONR⁵R⁶, -SO₂NR⁷R⁸, -C(=O)R¹³ and -XC(=O)R¹³;

or R² and R³, together with the carbons to which they are attached, form a four to seven membered monocyclic, or ten to fourteen membered bicyclic, carbocyclic ring that can be saturated or unsaturated, wherein from one to three of the nonfused carbon atoms of said monocyclic rings, and from one to five of the carbon atoms of said bicyclic rings that are not part of the benzo ring shown in formula I, may optionally and independently be replaced by a nitrogen,

oxygen or sulfur, and wherein said monocyclic and bicyclic rings may optionally be substituted with one or more substituents that are selected, independently, from (C₁-C₆) alkyl optionally substituted with from one to seven fluorine atoms, (C₁-C₆) alkoxy optionally substituted with from one to seven fluorine atoms, nitro, cyano, halo, (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, hydroxy, amino, (C₁-C₆) alkylamino and [(C₁-C₆) alkyl]₂amino, -CO₂R⁴, -CONR⁵R⁶, -SO₂NR⁷R⁸, -C(=O)R¹³ and -XC(=O)R¹³;

wherein each R⁴, R⁵, R⁶, R⁷, R⁸ and R¹³ is selected, independently, from hydrogen and (C₁-C₆) alkyl, or R⁵ and R⁶, or R⁷ and R⁸ together with the nitrogen to which they are attached, form a pyrrolidine, piperidine, morpholine, azetidine, piperazine, N-(C₁-C₆) alkylpiperazine or thiomorpholine ring, or a thiomorpholine ring wherein the ring sulfur is replaced with a sulfoxide or sulfone; with the proviso that when R¹ is hydrogen and R² is 4-hydroxy, then R³ is 5-(2-fluorobenzamidyl);

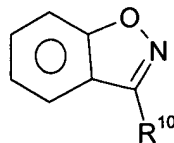
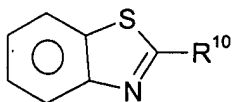
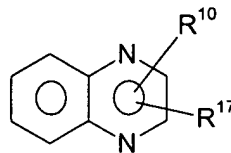
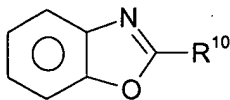
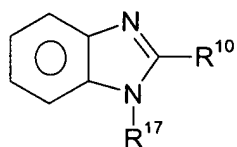
and

each X is, independently, (C₁-C₆) alkylene;

or a pharmaceutically acceptable salt thereof;

and a compound that is selected from a muscarinic agonist, ~~selected from the group consisting of 2-ethyl-8-methyl-2,8-diazaspiro-[4,5]-decan-1,3-diol hydrobromide, and an amyloid aggregation inhibitor, selected from the group consisting of 6-amidino-2-naphthyl-p-guanidinobenzoate dimethylsulfonate, and an estrogen-like therapeutic agent selected from the group consisting of estrogen.~~

2. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is, wherein R² and R³, together with the benzo ring of formula I, form a bicyclic ring system selected from the following:



wherein R^{10} and R^{17} are selected, independently, from (C_0-C_6) alkoxy- (C_0-C_6) alkyl- wherein the total number of carbon atoms does not exceed six and wherein any of the alkyl moieties may optionally be substituted with from one to seven fluorine atoms; nitro, cyano, halo, amino, (C_1-C_6) alkylamino-, $[(C_1-C_6) \text{ alkyl}]_2$ amino-, $-CO_2R^4$, $-CONR^5R^6$, $-SO_2NR^7R^8$, $-C(=O)R^{13}$, $-XC(=O)R^{13}$, phenyl and monocyclic heteroaryl, wherein said heteroaryl is selected from five to seven membered aromatic rings containing from one to four heteroatoms selected from oxygen, nitrogen and sulfur.

3. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is, wherein R^2 and R^3 do not, together with the benzo ring of formula I, form a bicyclic or tricyclic ring system.

4. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is, wherein one or both of R^2 and R^3 are $-C(=O)R^{13}$ wherein R^{13} is (C_1-C_6) alkyl.

5. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is, wherein one of R^2 and R^3 is $-COR^{13}$ wherein R^{13} is (C_1-C_6) alkyl or (C_1-C_3) alkyl optionally substituted with from one to seven fluorine atoms.

6. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is, wherein one of R^2 and R^3 is CF_3 , fluoro, cyano or C_2F_5 .

7. (canceled)

8. (previously presented) A method for reducing nicotine addiction or aiding in the cessation or lessening of tobacco use in a mammal, comprising administering to said mammal an amount of a pharmaceutical composition according to claim 1 that is effective in reducing nicotine addiction or aiding in the cessation or lessening of tobacco use.

9. (canceled)

10. (previously presented) A method for treating a disorder or condition selected from inflammatory bowel disease, ulcerative colitis, pyoderma gangrenosum, Crohn's disease, irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet

lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supranuclear palsy, chemical dependencies and addictions; dependencies on, or addictions to, nicotine, tobacco products, alcohol, benzodiazepines, barbiturates, opioids or cocaine; headache, stroke, traumatic brain injury (TBI), obsessive-compulsive disorder (OCD), psychosis, Huntington's Chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age related cognitive decline, epilepsy, petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome in a mammal, comprising administering to a mammal in need of such treatment a pharmaceutical composition according to claim 1 that is effective in treating such disorder or condition.

11. - 14. (canceled)

15. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is selected from the group consisting of
2-fluoro-N-(4-hydroxy-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-5-yl)-benzamide;
1-(10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;
and pharmaceutically acceptable salts thereof.

16. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is selected from the group consisting of:
4-methyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-nitro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-amino-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4,5-difluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-chloro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
3-(10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-5-methyl-1,2,4-oxadiazole;
10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-ol;
4,5-dichloro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
N⁴,N⁴-dimethyl-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-sulfonamide;
4-(1-pyrrolidinylsulfonyl)-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
4-ethynyl-5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
5-ethynyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
5-chloro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;

4-ethynyl-5-chloro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-fluoro-5-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-chloro-5-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
5-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
4-ethynyl-5-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4,5-bistrifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
and pharmaceutically acceptable salts thereof.

17. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is selected from the group consisting of:

3-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
3-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl cyanide;
4-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;

and pharmaceutically acceptable salts thereof.

18. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is:

4-nitro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene; or a pharmaceutically acceptable salt thereof.

19. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is:

4,5-dichloro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene; or a pharmaceutically acceptable salt thereof.

20. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is:

3-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene; or a pharmaceutically acceptable salt thereof.

21. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is:

3-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene; or a pharmaceutically acceptable salt thereof.

22. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is:

4-ethynyl-5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene; or a pharmaceutically acceptable salt thereof.

23. (previously presented) A pharmaceutical composition according to claim 1 wherein the compound of formula I is:

4-fluoro-5-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene; or a pharmaceutically acceptable salt thereof.

24. (canceled)

25. (previously presented) A pharmaceutical composition according to claim 1 wherein the neurotrophic factor is NGF.

26. (previously presented) A pharmaceutical composition according to claim 1 wherein the agent that slows or arrests Alzheimer's disease is a cognition enhancer.

27. (previously presented) A pharmaceutical composition according to claim 1 selected from the group consisting of:

5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

7-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

6-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

7-propyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

7-butyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

6-methyl-7-isobutyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

7-neopentyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

6-methyl-7-neopentyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;

6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;

and pharmaceutically acceptable salts thereof.

28. (previously presented) A pharmaceutical composition according to claim 1
which is:

6-methyl-5-thia-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
or a pharmaceutically acceptable salt thereof.

29. (previously presented) A pharmaceutical composition according to claim 1
which is:

6-methyl-7-propyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
or a pharmaceutically acceptable salt thereof.

30. (previously presented) A pharmaceutical composition according to claim 1
which is:

6, 7-dimethyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
or a pharmaceutically acceptable salt thereof.

31. (previously presented) A pharmaceutical composition according to claim 1
which is:

6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
or a pharmaceutically acceptable salt thereof.

32. (previously presented) A pharmaceutical composition according to claim 1
which is:

5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
or a pharmaceutically acceptable salt thereof.

33. (previously presented) A pharmaceutical composition according to claim 1
which is:

14-methyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
or a pharmaceutically acceptable salt thereof.

34. (previously presented) A pharmaceutical composition according to claim 1
which is:

5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
or a pharmaceutically acceptable salt thereof.

REPLY UNDER CFR 1.116
EXPEDITED PROCEDURE
GROUP ART UNIT 1624

Patent Application 10/075,348
Attorney Docket No. PC10030D

35. (previously presented) A pharmaceutical composition according to claim 1

which is:

7-methyl-5-oxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2,4(8),6,9-tetraene;

or a pharmaceutically acceptable salt thereof.